

## **Remarks**

Claims 1-3, 7-22, 24-28, 30, 33-35, 38, 57-59, and 61-74 were pending in the application. Claims 22, 24-28, 57, and 67-70 are allowed, and claims 2, 3, 7-12, 14-17, and 19 have been objected to as depending from a rejected claim. Claims 1, 13, 18, 20, 21, 30, 33-35, 38, 58, 59, 61-66, and 71-74 stand rejected. Claims 59, 61, or 62 are canceled by the present Amendment. Claims 1, 20, 30, 33, 38, 57, 65, 66, and 72 are amended as above. Support for the amendment to claim 57 wherein the oxime can be in the *E* or *Z* configuration can be found on page 31, lines 1-3, of the specification as originally filed. No new claims have been added. Applicant submits that no new matter has been added by these amendments. Applicant respectfully requests reexamination and reconsideration of the case, as amended. Each of the rejections levied in the Office Action is addressed individually below.

**I. Rejection under 35 U.S.C. § 112, first paragraph, for lack of enablement.** Claims 30, 33-35, 38, 59, 61-66, and 71-74 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention. The Examiner has maintained this rejection in spite of the arguments and references submitted with the last response, in support of claims drawn to Hsp90-dependent cancers. The Examiner states that Buchner and Roe are “speculative at best in the use of radicicol in its antitumor activity by disruption of Hsp-90 mediated activation of protein kinases.” The Examiner states that Yamamoto, Chiosis, and U.S.S.N. 60/531,092 are not persuasive in that the articles and provisional application were not public knowledge at the time of the filing. However, the Applicant submits that these references were not submitted as further teachings necessary for one of skill in the art to practice the claimed invention. Instead, they were submitted as evidence that the pharmaceutical compositions and methods as disclosed in the present invention are useful in the treatment of Hsp90-dependent cancers as described in the application as originally filed. No teachings from the Yamamoto, Chiosis, or the provisional application are needed to practice the invention. Applicant respectfully submits that the disclosure of the present application was not

insufficient, and the Applicant was not attempting to supplement with disclosure with the submitted references.

The rejected claims have now been amended with the present amendment to recite particular cancers (breast cancer, lung cancer, glioblastoma, and retinoblastoma) for which there is support in the present application. Applicant reserves the right to pursue the cancelled subject matter in future applications. Lung cancer, glioblastoma, and retinoblastoma are listed as cancers which are susceptible to the inventive compounds on page 58, lines 20-23 of the present application. Breast cancer is listed on page 59, line 28 as a cancer susceptible to the inventive compounds. Further evidence of the effectiveness of the inventive compounds in the treatment of these cancers is shown in Figures 17-21. Figures 17-20 show the results of *in vitro* studies on breast cancer cells lines, MCF7 and BT474. Figures 20 and 21 shows the results of *in vitro* testing of the inventive compounds on small cell lung carcinoma cell line, N417. Therefore, the Applicant respectfully submits that the claims are fully supported by the specification, and the Applicant requests the allowance of the claims as amended.

**II. Rejection under 35 U.S.C. § 102(b), as being anticipated by Sugimura *et al.*** Claims 1, 4, 13, 18, 21, 30, 33-35, 38, and 59-62 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Sugimura *et al.*, U.S. Patents 5,650,430 and 5,597,846. Examiner states that proviso (1) in claim 1 does not exclude all the compounds taught by Sugimura *et al.* In particular, the Examiner points to compounds wherein R<sub>B</sub> and R<sub>D</sub> are heteroarylalkyl. Proviso (1) of claim 1 has been amended to exclude these compounds. Particularly, the definitions of R<sub>B</sub> and R<sub>D</sub> in proviso (1) have been amended to include all possibilities for R<sub>B</sub> and R<sub>D</sub> as specified earlier in the claim. Applicant submits that all of the compounds taught by Sugimura *et al.* are excluded from the claimed invention since all the compounds have an –OR moiety or –COR moiety at R<sub>2</sub> or R<sub>4</sub> of the structure in claim 1 (*see* formula I and Table 1 of the ‘430 patent). Applicant respectfully requests that the rejection be removed.

**III. Rejection under 35 U.S.C. § 112, second paragraph, as being indefinite.** Claims 20, 30, 33-35, 38, 58, 59, 61-66, and 71-74 stand rejected under 35 U.S.C. § 112, second paragraph,

as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 30, 33-35, 38, 59, 61-66, and 71-74 have been rejected by the Examiner for being indefinite, "in that it is not known which diseases are capable of being responsive to the activity of Hsp90." The Applicant disagrees with the Examiner's assessment of the claims and respectfully submits that the scope of diseases and disorders associated with Hsp90 is not indefinite. However, solely in order to further prosecution, the Applicant has amended the claims to recite particular cancers. The present Amendment, therefore, renders the Examiner's rejection moot.

Claim 20 has been rejected by the Examiner for insufficient antecedent basis for the limitation "lower alkyl" in the definition of R<sub>5</sub> and R<sub>6</sub>. "Lower alkyl" has been removed from this definition rendering the Examiner's rejection moot.

Claim 58 stands rejected by the Examiner. The Examiner states that claim 58 is a duplicate of claim 22; however, this is incorrect. The structure shown in claim 22 has an epoxide ring at position A and B, whereas the structure shown in claim 58 has a cyclopropyl ring at this position. Therefore, the claims are not duplicates. Applicant respectfully requests that the rejection be removed,

In view of the forgoing amendments and arguments, Applicant respectfully submits that the present case is now in condition for allowance. A Notice to that effect is requested.

Please charge any fees that may be required for the processing of this Response, or credit any overpayments, to our Deposit Account No. 03-1721.

Respectfully submitted,



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